

*Amendments to the Claims*

The listing of claims will replace all prior versions, and listings of claims in the application.

1-60. (cancelled)

61. (currently amended) A comparative high throughput, parallel screening method of determining for comparing the pharmacological effects of test substances on the activities of different biological target molecules contained in test cells of the same type, said method comprising:

- (a) selecting from a cell population test cells of the same type which contain different biological target molecules;
- ~~(b) applying test substances in parallel to sets of said test cells selected in (a);~~  
~~wherein a defined amount of a test substance from the same supply is~~  
~~applied simultaneously to a set of said test cells containing different~~  
~~biological target molecules;~~
- (b) applying under the control of a robot test substances in parallel to sets of  
said test cells selected in (a), wherein a test substance is applied  
simultaneously in a defined amount and from the same supply to a set of  
said test cells, said set comprising test cells selected in (a) of the same  
type which contain different biological target molecules;
- (c) measuring the effects of said test substances applied in (b) on the biological activities of said different biological target molecules using a

~~detection system using different assays or assay formats~~ a detection system, wherein (i) said detection system is coupled to activation of said different biological target molecules, or (ii) said detection system is coupled to one or more regulatory mechanisms triggered by activation of said different biological target molecules; and

- (d) directly or indirectly comparing with one another the effects of said test substances on said biological activities of said different biological target molecules measured in (c);

wherein said biological target molecules are components of metabolic or receptor-coupled signal transduction pathways.

62. (cancelled)

63. (previously presented) The method of claim 61, wherein said different target molecules include Ras, Bcl-2 or Raf, or any combination thereof.

64. (previously presented) The method of claim 63, wherein said different target molecules include Ras.

65. (previously presented) The method of claim 63, wherein said different target molecules include Bcl-2.

66. (previously presented) The method of claim 63, wherein said different target molecules include Raf.

67. (previously presented) The method of claim 61, wherein said target molecules are selected from components of a receptor-coupled signal transduction pathway.

68. (previously presented) The method of claim 61, wherein said different target molecules are selected from the group consisting of

- (i) receptor tyrosine kinases, serine/threonine kinases, integrin receptors, receptors of class LIF,
- (ii) oncostatin M, CNTF, gp130,
- (iii) receptor phosphatases, cytokine receptors, G-protein coupled receptors, neurokinin receptors,
- (iv) serotonin receptors, and
- (v) any combination thereof.

69. (previously presented) The method of claim 67, wherein said different target molecules include EGF receptor, HGF receptor, HER2, KDR, neurokinin-1 receptor, neurokinin-2 receptor, or serotonin 5HT<sub>2</sub> receptor, or any combination thereof.

70. (previously presented) The method of claim 69, wherein said different target molecules include EGF receptor.

71. (previously presented) The method of claim 69, wherein said different target molecules include HGF receptor.

72. (previously presented) The method of claim 69, wherein said different target molecules include HER2.

73. (previously presented) The method of claim 69, wherein said different target molecules include KDR.

74. (previously presented) The method of claim 69, wherein said different target molecules include neurokinin-1 receptor.

75. (previously presented) The method of claim 69, wherein said different target molecules include neurokinin-2 receptor.

76. (previously presented) The method of claim 69, wherein said different target molecules include serotonin 5HT<sub>2</sub> receptor.

77. (previously presented) The method of claim 61, wherein said biological activity is an activity responsible for one or more pathological effects.

78. (previously presented) The method of claim 77, wherein said biological activity is proliferation or apoptosis.

79. (previously presented) The method of claim 78, wherein said biological activity is proliferation.

80. (previously presented) The method of claim 78, wherein said biological activity is apoptosis.

81. (previously presented) The method of claim 61, wherein said test cells are transformed with DNA operably encoding said different target molecules.

82. (previously presented) The method of claim 81, wherein said different target molecules are receptors.

83. (previously presented) The method of claim 61, wherein said detection system is selected from a group consisting of a proliferation assay, an apoptosis assay, a reporter gene expression system, and any combination thereof.

84. (previously presented) The method of claim 83, wherein said reporter gene is selected from the group consisting of luciferase, green fluorescent protein, alkaline phosphatase,  $\beta$ -glucuronidase, chloramphenicol-acetyltransferase, and any combination thereof.

85. (previously presented) The method of claim 84, wherein said reporter gene is luciferase.

86. (previously presented) The method of claim 84, wherein said reporter gene is green fluorescent protein.

87. (previously presented) The method of claim 61, wherein said test cells are mammalian cells.

88. (previously presented) The method of claim 87, wherein said test cells are human cells.

89. (previously presented) The method of claim 61, wherein said test cells have the same genotype.

90. (currently amended) A comparative high throughput, parallel screening method of ~~determining for comparing~~ the pharmacological effects of test substances on the activity of the same biological target molecule contained in test cells of different types or of the same type but with a different state of differentiation or activation, said method comprising:

- (a) selecting from a cell population test cells of different types which contain the same biological target molecule, or test cells of the same type but with

a different state of differentiation or activation which contain the same biological target molecule;

- (b) applying under the control of a robot test substances in parallel to ~~one or more~~ sets of said test cells selected in (a), wherein a defined amount of a test substance from the same supply is applied simultaneously to (i) a set of said test cells, said set comprising (i) said test cells selected in (a) of different types which contain the same biological target molecule, or (ii) a set of said said test cells selected in (a) of the same type but with a different state of differentiation or activation which contain the same biological target molecule;
- (c) measuring the effects of said test substances applied in (b) on the biological activity of said target molecule using ~~a detection system using different assays or assay formats~~ a detection system, wherein (i) said detection system is coupled to activation of said biological target molecule, or (ii) said detection system is coupled to a regulatory mechanism triggered by activation of said biological target molecule;
- (d) directly or indirectly comparing with one another the effects of said test substances on the biological activity of said target molecule measured in (c);

wherein said biological target molecule is a component of a metabolic or a receptor-coupled signal transduction pathway.

91. (cancelled)

92. (previously presented) The method of claim 90, wherein said target molecule is selected from the group consisting of Ras, Bcl-2, and Raf.

93. (previously presented) The method of claim 92, wherein said target molecule is Ras.

94. (previously presented) The method of claim 92, wherein said target molecule is Bcl-2.

95. (previously presented) The method of claim 92, wherein said target molecule is Raf.

96. (previously presented) The method of claim 90, wherein said target molecule is selected from components of a receptor-coupled signal transduction pathway.

97. (previously presented) The method of claim 90, wherein said target molecule is selected from the group consisting of

(i) receptor tyrosine kinases, serine/threonine kinases, integrin receptors, receptors of class LIF,

(ii) oncostatin M, CNTF, gp130,



(iii) receptor phosphatases, cytokine receptors, G-protein coupled receptors, neurokinin receptors, and

(iv) serotonin receptors.

98. (previously presented) The method of claim 96, wherein said target molecule is selected from the group consisting of EGF receptor, HGF receptor, HER2, KDR, neurokinin-1 receptor, neurokinin-2 receptor, and serotonin 5HT<sub>2</sub> receptor.

99. (previously presented) The method of claim 98, wherein said target molecule is EGF receptor.

100. (previously presented) The method of claim 98, wherein said target molecule is HGF receptor.

101. (previously presented) The method of claim 98, wherein said target molecule is HER2.

102. (previously presented) The method of claim 98, wherein said target molecule is KDR.

103. (previously presented) The method of claim 98, wherein said target molecule is neurokinin-1 receptor.

104. (previously presented) The method of claim 98, wherein said target molecule is neurokinin-2 receptor.

105. (previously presented) The method of claim 98, wherein said target molecule is serotonin 5HT<sub>2</sub> receptor.

106. (previously presented) The method of claim 90, wherein said biological activity is an activity responsible for one or more pathological effects.

107. (previously presented) The method of claim 106, wherein said biological activity is proliferation or apoptosis.

108. (previously presented) The method of claim 107, wherein said biological activity is proliferation.

109. (previously presented) The method of claim 107, wherein said biological activity is apoptosis.

110. (previously presented) The method of claim 90, wherein said target cells are transformed with DNA operably encoding said target molecule.

111. (previously presented) The method of claim 110, wherein said target molecule is a receptor.

112. (previously presented) The method of claim 90, wherein said detection system is selected from a group consisting of a proliferation assay, an apoptosis assay, a reporter gene expression system, and any combination thereof.

113. (previously presented) The method of claim 112, wherein said reporter gene is selected from the group consisting of luciferase, green fluorescent protein, alkaline phosphatase,  $\beta$ -glucuronidase, and chloramphenicol-acetyltransferase.

114. (previously presented) The method of claim 113, wherein said reporter gene is luciferase.

115. (previously presented) The method of claim 113, wherein said reporter gene is green fluorescent protein.

116. (previously presented) The method of claim 90, wherein said test cells are mammalian cells.

117. (previously presented) The method of claim 116, wherein said test cells are human cells.

118. (previously presented) The method of claim 90, wherein said test cells are from different cell types.

119. (previously presented) The method of claim 90, wherein said test cells are of the same type, but with different states of differentiation or activation.

120. (previously presented) The method of claim 119, wherein said test cells are tumor cells and normal cells.

121. (previously presented) The method of claim 61, wherein said test cells are clonally selected from a single cell.

122. (previously presented) The method of claim 90, wherein said test cells are clonally selected from a single cell.

123. (previously presented) The method of claim 61, wherein said test cells are selected by antibiotic resistance.

124. (previously presented) The method of claim 123, wherein said antibiotic resistance is G-418 resistance.

125. (previously presented) The method of claim 90, wherein said test cells are selected by antibiotic resistance.

126. (previously presented) The method of claim 125, wherein said antibiotic resistance is G-418 resistance.